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DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI; PLUR=YES; OP=ADJ			
L22	l9 with carrier	14	L22
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L18	dna or nucleic	236614	L18
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L14	l9 with (dna or nucleic or polynucleotide or vector or carrier)	32	L14
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L9	albumine	568	L9

L8	L7 same l2	52	L8
L7	L6 with (polymer or microparticles or matrix or PLGA)	24518	L7
L6	trehalose or sugar or lactose or polyssacharides or saccharides or glucose	379165	L6
L5	PLGA with (DPPC or phosphatidylcholine or fatty acid)	15	L5
L4	l2 and l1	24	L4
L3	L2 same l1	4	L3
L2	DPPC or phosphatidylcholine	11671	L2
L1	PLGA with(sugar or polysaccharides or saccharides or lactose or trehalose)	84	L1

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L5: Entry 2 of 15 File: PGPB Apr 22, 2004

DOCUMENT-IDENTIFIER: US 20040076589 A1
TITLE: Highly efficient delivery of a large therapeutic mass aerosol

Detail Description Paragraph:
[0064] Surface eroding polymers such as polyanhydrides may be used to form the particles. For example, polyanhydrides such as poly[(.rho.-carboxyphenoxy)-hexane anhydride] (PCPH) may be used. Biodegradable polyanhydrides are described in U.S. Pat. No. 4,857,311. Bulk eroding polymers such as those based on polyesters including poly(hydroxy acids) also can be used. For example, polyglycolic acid (PGA), polylactic acid (PLA), or copolymers thereof may be used to form the particles. The polyester may also have a charged or functionalizable group, such as an amino acid. In a preferred embodiment, particles with controlled release properties can be formed of poly(D,L-lactic acid) and/or poly(D,L-lactic-co-glycolic acid) ("PLGA") which incorporate a surfactant such as dipalmitoyl phosphatidylcholine (DPPC).

L5: Entry 10 of 15 File: USPT Jul 1, 2003

DOCUMENT-IDENTIFIER: US 6586008 B1
TITLE: Use of simple amino acids to form porous particles during spray drying

Brief Summary Text (47):
In another embodiment, bulk eroding polymers such as those based on polyesters including poly(hydroxy acids) can be used. For example, polyglycolic acid (PGA), polylactic acid (PLA), or copolymers thereof may be used to form the particles. The polyester may also have a charged or functionalizable group, such as an amino acid. In a preferred embodiment, particles with controlled release properties can be formed of poly(D,L-lactic acid) and/or poly(D,L-lactic-co-glycolic acid) ("PLGA") which incorporate a phospholipid such as DPPC.

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L5: Entry 11 of 15 File: USPT Aug 21, 2001

DOCUMENT-IDENTIFIER: US 6277413 B1
TITLE: Biodegradable compositions for the controlled release of encapsulated substances

Detailed Description Text (41):
The solvent phase contained either the polymer poly(DL-lactide-glycolide) (PLGA) alone at a concentration of 250 mg/mL, or a mixture of PLGA, dioleoyl phosphatidylcholine (DOPC), dipalmitoyl phosphatidylglycerol (DPPG), cholesterol and triolein at concentrations of 22.4 mg/mL, 10.4 mg/mL, 2.1 mg/mL, 7.7 mg/mL, and 2.2 mg/mL, respectively. PLGA was from Sigma Chemical Company (St. Louis, Mo.), with a lactide:glycolide ratio of 50:50 and a molecular weight of 40,000-75,000. This material (with lactide:glycolide of 1:1) was used in all experiments, except where indicated (in Example 4). DOPC, DPPG, and triolein were from Avanti Polar Lipids (Alabaster, Ala.), and cholesterol was from Spectrum Chemical Manufacturing Corp. (Gardena, Calif.). This corresponds to a solvent phase either with polymer alone, or with lipids and polymer in a 1:1 weight ratio. The ratios of the volume of the aqueous phase to the volume of the volatile organic solvent phase are given in Table 1. The "water-in-oil" emulsion was prepared by mixing on a Homo Mixer (Tokushu Kika Kogyo Co., Ltd., Osaka, Japan) at a speed of 9,600 rpm for 20 min. The second aqueous phase was either 4% wt. polyvinyl alcohol (PVA) for comparative formulations, water, or a mixture of 5% wt. glucose and 40 mM lysine. Spherules were formed by mixing at 4,000 rpm for 1 min. The suspending medium was exchanged with 0.9% wt. sodium chloride by washing and centrifuging at 600.times.g twice.

Detailed Description Text (114):
The pharmaceutical compositions were prepared by employing a double emulsification process. The "water-in-oil" type emulsion was prepared from 5 mL of 25 mM arginine-glycine-glycine (Sigma, St. Louis, Mo.) buffer pH 7.9 containing 4 percent dextrose (Fisher, Fair Lawn, N.J.), and erythropoietin with 2.5 mg/mL human serum albumin (gift from UC San Diego Medical Center, San Diego, Calif.). The volatile organic phase contained lipids and polymer at a ratio of 1:1, with or without erythropoietin, or lipid/polymer ratio of 4:1 with erythropoietin. The water-immiscible solvent phase contained a mixture of phospholipids, cholesterol, triglycerides and PLGA (poly DL-lactide-co-glycolide). For the 1:1 (mass of lipid:mass of polymer) formulation, the solvent phase contained 10.4 mg/mL DOPC (dioleoyl phosphatidylcholine), 2.1 mg/mL DPPG (dipalmitoyl phosphatidylglycerol, sodium salt), 2.2 mg/mL triolein, all from Avanti Polar Lipids (Alabaster, Ala.), 7.7 mg/mL cholesterol (Spectrum, Garden, Calif.), and 22.4 mg/mL PLGA (Sigma, St. Louis, Mo.) dissolved in chloroform (Spectrum, Gardena, Calif.). For the 4:1 formulation the weight ratio of lipid to polymer was varied, keeping the total concentration of lipid plus polymer constant. The mixing speed and time for producing the "water-in-oil" type emulsion was 9,000 rpm for 8 minutes on a Homo Mixer (Tokoshu Kika Kogyo Co., Ltd., Osaka, Japan). The second aqueous phase was 20 mL of a solution containing 4% glucose (McGaw, Irvine, Calif.) and 40 mM lysine (Degussa, Courbevoie, France). The second aqueous phase was added to the "water-in-oil" suspension and mixed at 4,000 rpm for 1 minute. The organic solvent was removed by slow shaking at 37.degree. C. with nitrogen gas passing at 50 liters/minute for 20 minutes. The suspending medium was exchanged with 25 mM argenine-glycine-glycine buffer pH 7.9 by washing and centrifuging at 600.times.g twice.

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L5: Entry 12 of 15 File: USPT Feb 13, 2001

DOCUMENT-IDENTIFIER: US RE37053 E
** See image for Certificate of Correction **
** See image for Reexamination Certificate **
TITLE: Particles incorporating surfactants for pulmonary drug delivery

Drawing Description Text (2):
FIG. 1 is a graph comparing the mass fraction of the initial dose that is released from a dry powder inhaler device, after in vitro aerosolization of poly (D,L-lactic-co-glycolic acid) ("PLGA") microspheres made by a double emulsion procedure with and without the incorporation of L-.alpha.-phosphatidylcholine dipalmitoyl ("DPPC").

Drawing Description Text (3):
FIG. 2 is a graph comparing the mass fraction of the aerosolized dose that is deposited in different stages of a cascade impactor after in vitro aerosolization of PLGA microspheres made by a double emulsion procedure with and without the incorporation of DPPC.

Drawing Description Text (4):
FIG. 3 is a graph showing the aerosolization behavior of PLGA microspheres made by spray drying with and without the incorporation of DPPC showing the mass-fraction of the initial dose that is released from the dry powder inhaler device after in vitro aerosolization.

Drawing Description Text (5):
FIG. 4 is a graph comparing the in vitro aerosolization behaviors of PLA and PLGA microspheres made by spray drying with and without the incorporation of DPPC showing the mass-fraction of the aerosolized dose that is deposited in stages of a cascade impactor corresponding to the "respirable-fraction".

Detailed Description Text (14):
In another embodiment, bulk eroding polymers such as those based on polyesters including poly(hydroxy acids) can be used. For example, polyglycolic acid (PGA), polylactic acid (PLA), or copolymers thereof may be used to form the particles. The polyester may also have a charged or functionalizable group, such as an amino acid. In a preferred embodiment, particles with controlled release properties can be formed of poly(D,L-lactic acid) and/or poly(D,L-lactic-co-glycolic acid) ("PLGA") which incorporate a surfactant such as DPPC.

Detailed Description Text (103):
where d.sub.resp corresponds to the diameter of particles (in .mu.m) theoretically able to enter and remain in the airways without inertial or gravitational deposition (particles smaller than this range are exhaled), and where .rho..sub.MS is in units of g/cc. The theoretical respirable size range of the microspheres also is shown in Table 2. The optimal size range (i.e., d.sub.resp) for a non-porous PLGA 50:50 microsphere is 0.69-4.05 .mu.m (Table 2). The optimal respirable size range for microspheres without DPPC is 1.3-7.7 .mu.m and, for microspheres with DPPC, 1.46-8.58 .mu.m (Table 2). The upper limit on size of respirable particles is increased from 4.05 to greater than 8.5 .mu.m when DPPC is used in the PLGA microsphere preparation. Therefore, the use of low density DPPC microspheres allows

the use of larger particles for aerosolization, which may have advantages for drug delivery, such as less particle-particle interaction due to decreased surface area to volume ratio, and lower susceptibility to phagocytosis by alveolar macrophages. In addition, a primary effect of DPPC is to render the particles less adhesive and therefore allow improved aerosolization, as demonstrated below.

Detailed Description Text (104):
FIGS. 1 and 2 show the results of an in vitro aerosolization of the PLGA microspheres made by a double emulsion process with and without DPPC. The microspheres were aerosolized as a dry powder released from a Spinhaler.RTM. dry powder inhaler (DPI). FIG. 1 illustrates the mass-fraction of the initial dose that is released from the dry powder inhaler device (DPI Efficiency) using an Andersen Mark I Cascade Impactor. DPI efficiencies approaching 80% were obtained with microspheres made with and without DPPC. Although the DPI efficiencies for the two batches were nearly the same, a great difference can be seen between microspheres made with and without DPPC when their deposition within the cascade impactor is observed (FIG. 2).

Detailed Description Text (107):
To determine whether agglomeration forces during particle aerosolization from the Spinhaler device might be playing a role even after the particles enter the impactor system (i.e., primarily non-DPC particles remain agglomerated in the inspired stream, resulting in deposition in the first two impactor stages: stages 0 and 1), in vivo aerosolization experiments were performed in which particles were permitted to fall by gravity into the inspiration stream of a Harvard ventilator system joined with the trachea of an anesthetized rate. In this model, approximately 63% of the inhaled DPPC-PLGA particles deposit in the airways and distal lung regions, whereas 57% of the non-DPPC particles are able to penetrate beyond the trachea in the lungs. These respirable fractions are much nearer to the predicted respirable fractions based upon particle diameter and mass density (Table 3).

Detailed Description Text (108):
Particle aggregation thus is less with DPPC-containing PLGA particles than without DPPC, even though the particles are of similar size and surface morphological features. The use of DPPC thus appears to reduce interparticle attractions, such as van der Waals and electrostatic attractions. It is also possible that the presence of DPPC reduces moisture absorption which may cause particle-particle interaction by capillary forces.

Detailed Description Text (109):
In addition to the biocompatibility features of DPPC and improvement of surface properties of microspheres for aerosolization, it is possible that the release of DPPC from the slow-eroding PLGA microspheres in the alveolar region of the lungs can more effectively insure the maintenance of normal surfactant fluid composition thereby minimizing the possibility of local toxic side effects. The alveolar surfactant fluid layer is, on average, 10 nm thick (Weibel, E. R., Morphometry of the Human Lung, New York: Academic Press (1963).

Detailed Description Text (113):
Aerosolization properties of the microspheres also were examined, as shown in Table 5. Microspheres made by spray drying with and without DPPC have similar size distributions (Table 5) and mass densities (0.49.+-.0.04 g/cc). However, the aerosolization performance of spray-dried aerosols made with and without DPPC is markedly different. FIG. 3 shows that the fraction of low-molecular-weight PLGA RG503 microparticles that are aerosolized from the dry powder inhaler (i.e., the % of particles that leave the DPI upon simulated inhalation, defined as the DPI Efficiency) is 70.4% when the particles are made with DPPC compared with only 46.8% for particles made without DPPC. Furthermore, the deposition of all types of polymer microparticles following aerosolization into an Andersen impactor is

greatly improved using DPPC-coated particles (Table 5). Without the use of DPPC, .ltoreq.2% of the particles aerosolized reach the latter stages of the impactor (those corresponding to the respirable fraction, stages 2-Filter). On the other hand, a maximum of 25.6% of DPPC-coated microspheres reach stages 2-Filter, as shown in FIG. 4. Higher respirable fractions may be obtained with particles that contain low molecular weight drugs that are soluble in methylene chloride and therefore do not require the use of water during their preparation.

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L5: Entry 15 of 15 File: USPT Nov 17, 1998

DOCUMENT-IDENTIFIER: US 5837221 A
TITLE: Polymer-lipid microencapsulated gases for use as imaging agents

Detailed Description Text (63):
Preparation of Octafluoropropane PEG-PLGA/PLGA microparticles with dipalmitoylphosphatidylcholine (DPPC).

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L8: Entry 18 of 52 File: PGPB Oct 18, 2001

DOCUMENT-IDENTIFIER: US 20010031740 A1
TITLE: Methods for delivering compounds into a cell

CLAIMS:

39. A method of claim 2 wherein said carrier is selected from the group consisting of dioleoylphosphatidylethanolamine, a fatty acid, a lysolipid, phosphatidylcholine, phosphatidylethanolamine, phosphatidylserine, phosphatidylglycerol, phosphatidylinositol, a sphingolipid, a glycolipid, a glucolipid, a sulfatide, a glycosphingolipid, phosphatidic acid, palmitic acid, stearic acid, arachidonic acid, oleic acid, a lipid bearing a polymer, a lipid bearing a sulfonated saccharide, cholesterol, tocopherol hemisuccinate, a lipid with an ether-linked fatty acid, a lipid with an ester-linked fatty acid, a polymerized lipid, diacetyl phosphate, stearylamine, cardiolipin, a phospholipid with a fatty acid of 6-8 carbons in length, a phospholipid with asymmetric acyl chains, 6-(5-cholesten-3b-yloxy)-1-thio-b-D-galactop- yranoside, digalactosyldiglyceride, 6-(5-cholesten-3b-yloxy)hexyl-6-amino-- 6-deoxy-1-thio-b-D-galactopyranoside, 6-(5-cholesten-3.beta.-yloxy)hexyl-6- -amino-6-deoxyl-1-thio-60 -D-mannopyranoside, 12-(((7'-diethylamino-coumar- in-3-yl)carbonyl)methylamino)-octadecanoic acid; N-[12-(((7'-diethylaminoc- oumarin-3-yl)carbonyl)methyl-amino) octadecanoyl]-2-aminopalmitic acid; cholesteryl)4'-trimethyl-ammonio)butanoate; N-succinyldioleoyl-phosphatid- ylethanolamine; 1,2-dioleoyl-sn-glycerol; 1,2-dipalmnitoyl-sn-3-succinyl-g- lycerol; 1,3-dipalmitoyl-2-succinylglycerol; 1-hexadecyl-2-palmitoylglycer- ophosphoethanolamine, palmitoylhomocysteine, and/or combinations thereof.

L8: Entry 22 of 52 File: USPT Feb 3, 2004

DOCUMENT-IDENTIFIER: US 6685669 B2
TITLE: Particle delivery

Detailed Description Text (9):
Particles of a therapeutic agent, alone or in combination with other drugs or agents, are typically prepared as pharmaceutical compositions which can contain one or more added materials such as carriers, vehicles, and/or excipients. "Carriers," "vehicles" and "excipients" generally refer to substantially inert materials which are nontoxic and do not interact with other components of the composition in a deleterious manner. These materials can be used to increase the amount of solids in particulate pharmaceutical compositions. Examples of suitable carriers include silicone, gelatin, waxes, and like materials. Examples of normally employed "excipients," include pharmaceutical grades of dextrose, sucrose, lactose, trehalose, mannitol, sorbitol, inositol, dextran, starch, cellulose, sodium or calcium phosphates, calcium sulfate, citric acid, tartaric acid, glycine, high molecular weight polyethylene glycols (PEG), erodible polymers (such as polylactic acid, polyglycolic acid, and copolymers thereof), and combinations thereof. In addition, it may be desirable to include a charged lipid and/or detergent in the pharmaceutical compositions. Such materials can be used as stabilizers, anti-oxidants, or used to reduce the possibility of local irritation at the site of administration. Suitable charged lipids include, without limitation, phosphatidylcholines (lecithin), and the like. Detergents will typically be a nonionic, anionic, cationic or amphoteric surfactant. Examples of suitable surfactants include, for example, Tergitol.RTM. and Triton.RTM. surfactants (Union Carbide Chemicals and Plastics, Danbury, Conn.), polyoxyethylenesorbitans, e.g., TWEEN.RTM. surfactants (Atlas Chemical Industries, Wilmington, Del.), polyoxyethylene ethers, e.g., Brij, pharmaceutically acceptable fatty acid esters, e.g., lauryl sulfate and salts thereof (SDS), and like materials.

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L8: Entry 34 of 52 File: USPT Mar 20, 2001

DOCUMENT-IDENTIFIER: US 6204054 B1
** See image for Certificate of Correction **
TITLE: Transcytosis vehicles and enchancers for drug delivery

Brief Summary Text (36):
In particular, a transcytosis enhancer or vehicle of the present invention or a mixture thereof, preferably at a concentration of about 20% w/v, is used for spray-drying. The preparation to be sprayed may contain substances other than the transcytosis enhancers or vehicles and solvent or carrier liquid. For example, the aqueous phase may contain 1-20% by weight of water-soluble hydrophilic compounds such as sugars and polymers as stabilizers, e.g., polyvinyl alcohol (PVA), polyvinyl pyrrolidone (PVP), polyethylene glycol (PEG), gelatin, polyglutamic acid and polysaccharides such as starch, dextran, agar, xanthin and the like. Similar aqueous phases can be used as the carrier liquid in which the final microsphere product is suspended before use. Emulsifiers may be used (0.1-5% by weight), including most physiologically-acceptable emulsifiers, for instance egg lecithin or soya bean lecithin, or synthetic lecithins such as saturated synthetic lecithins, for example, dimyristoyl phosphatidylcholine, dipalmitoyl phosphatidylcholine, or distearoyl phosphatidylcholine or unsaturated synthetic lecithins, such as dioleyl phosphatidylcholine or dilinoleyl phosphatidylcholine. Emulsifiers also include surfactants such as free fatty acids, esters of fatty acids with polyoxyalkylene compounds, e.g. polyoxypropylene glycol and polyoxyethylene glycol; ethers of fatty alcohols with polyoxyalkylene glycols; esters of fatty acids with polyoxyalkylated sorbitan; soaps; glycerol-polyoxyethylene ricinoleate; homo-and copolymers of polyalkylene glycols; polyethoxylated soya-oil and castor oil as well as hydrogenated derivative; ethers and esters of sucrose or other carbohydrates with fatty acids, fatty alcohols, these being optionally polyoxyalkylated; mono-, di- and triglycerides of saturated or unsaturated fatty acids, glycerides or soya-oil and sucrose.

L8: Entry 47 of 52 File: USPT Jul 7, 1998

DOCUMENT-IDENTIFIER: US 5776488 A
TITLE: Liposome preparation

Brief Summary Text (6):
Of such studies, a method comprising encapsulating an anti-malignant tumor agent in liposomes has been known, which utilizes the tendency, when compared to normal tissues, of malignant tumor tissues toward easy uptake of microparticles, such as liposomes, which are fine and closed vesicles having a lipid bilayer structure formed upon dispersion of phospholipids or glycolipids in aqueous solutions. Encapsulation of an anti-malignant tumor agent in liposomes has revealed high anti-malignant tumor effects resulting from the suppression of adverse influences on normal cells and possible consecutive administration of the agent in large doses. Yet, mere formulation into liposomes does not suppress migration of an anti-malignant tumor agent to myeloid tissues, nor does it allow sufficient accumulation of the agent in malignant tumor tissues. Thus, an attempt has been made to prolong residence of the agent in blood by various modifications of liposomes, whereby to ultimately accumulate the anti-malignant tumor agent in malignant tumor tissues. Such attempt includes (1) decreasing the particle size of liposomes [Cancer Research, vol 36, pp. 2949-2957 (1976)], (2) using a liposome membrane structure-reinforcing factor such as phosphatidylcholine having long chain saturated fatty acid [Biochimica et Biophysica Acta, vol. 839, pp. 1-8 (1985)], (3) adding a synthetic lipid of a water-soluble polymer (e.g., polyethylene glycol), a natural polysaccharide or a sugar which has been bound with fatty acid, cholesterol, etc. [Biochimica et Biophysica Acta, vol. 1113, pp. 171-199 (1992), and Oyo Saibo Seibutsugaku Kenkyu, vol. 9 (3-4), pp. 53-61 (1992)] and other methods, and the third method in fact has achieved accumulation in malignant tumor tissues. However, no report has documented a successful suppression of migration of an anti-malignant tumor agent to myeloid tissues, the site of expression of side effects caused by the anti-malignant tumor agent, and the problem regarding the expression of myelotoxicity has not been resolved.

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L12: Entry 48 of 53 File: EPAB Oct 29, 1986

DOCUMENT-IDENTIFIER: GB 2174097 A
TITLE: Polymeric stabilizer of water-in-oil emulsions

Abstract Text (2):
The preparations of spherical microparticles of starch, dextran or human serum albumine using the above stabilizer are described.